SPACEFLIGHT DID NOT IMPAIR CARDIOVASCULAR RESPONSES TO UPRIGHT POSTURE IN AN ELDERLY ASTRONAUT

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TECH. RVW.:
CONTENT
WELL-ORGANIZED
CLEARLY PRESENTED
WELL-RESEARCHED BACKGROUND

COMMENTS (NO BIGGIES)

COLOR BARS FOR SUPINE & STANDING DATA LEGENDS APPEARED AS SAME COLOR, ALTHO DATA BARS WERE DIFFERENT, & OBVIOUS FROM CONTEXT

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FORM 548 - PAPER REVERSED, DOES NOT TRANSMIT SIGNATURE.

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Running title: An elderly astronaut's responses to spaceflight.

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ABSTRACT

Some of the cardiovascular changes associated with spaceflight have similarities to those associated with aging. We studied the neuroendocrine and hemodynamic responses to upright posture in a 77 year old astronaut before and after spaceflight and compared them to those of a group of 20 younger (41 ± 1 years) astronauts. While arterial pressure responses to standing were similar between the young and old astronauts, hemodynamic profiles were quite different. The elderly astronaut achieved adequate standing arterial pressure primarily by maintaining stroke volume and thus cardiac output. In spite of very high norepinephrine release, he had very little increase in heart rate or total peripheral resistance. This pattern persisted on all test occasions. These responses suggest high sympathetic responses, down-regulated adrenergic receptors and decreased venous compliance typical of aging. In contrast, younger astronauts did not maintain stroke volume or cardiac output with standing, but had significant increases in heart rate and resistance. These results suggest that this elderly subject had cardiovascular responses to standing that are expected in an aged person. These responses were not deleteriously affected by spaceflight. We suggest that healthy, fit elderly individuals are able to withstand the stresses of extreme environments and are not necessarily limited in their activities simply due to their chronological age.

Key words: aging, geriatric, microgravity, tilt test

INTRODUCTION

During spaceflight the human body undergoes profound adaptations which affect virtually all physiologic systems. The cardiovascular system undergoes changes which result most consistently in orthostatic hypotension and syncope or presyncope after landing. During the last four decades some degree of insight into the mechanisms of the cardiovascular changes associated with spaceflight has been gained. It has been shown that losses of plasma volume (1), development of autonomic dysfunction (2-4), and vascular changes (5,6) probably all contribute to postflight orthostatic hypotension. The normal aging process is associated with patterns of autonomic and vascular changes that are similar in some ways to those associated with spaceflight. However, changes associated with spaceflight reverse spontaneously without intervention, while those associated with aging do not. Most astronauts are of very similar ages at the time of their spaceflights, so virtually no data are available on the effects of spaceflight on older individuals. Recently we were afforded the opportunity to document cardiovascular responses to standing before and after a ten day spaceflight in an elderly male (77 years old), and compare them to those previously documented in younger male astronauts. This study represents the only evaluation of cardiovascular changes associated with spaceflight in an elderly individual.

METHODS:

This study was approved by The Johnson Space Center Investigational Review Board. Data were collected ten days prior to launch, two hours after landing and three days after landing on a ten day spaceflight. The subject of this investigation was a 77 year old healthy male astronaut. Prior to each test, the subject had abstained from caffeine, alcohol and any medication for the preceding 12 hours, was at least two hours post-prandial and had not exercised heavily in 24 hours. The subject was laid on a tilt table, and instrumented for ECG, manual blood pressure (sphygmomanometer) and finger arterial pressure (Finapres, Ohmeda, Inglewood, Co). A catheter was inserted into an antecubital vein. After a 20 minute supine rest period, a blood sample was drawn for determination of plasma norepinephrine and epinephrine levels. Then plasma volume was determined using carbon monoxide rebreathing (7-9). Two dimensional and M-mode echocardiography were used to determine aortic cross sectional diameter and Doppler ultrasound was used to measure beat-to-beat aortic flows. The hand to which the Finapres was attached was strapped to an arm board so that it would remain at heart level in both the supine and upright positions. Continuous baseline measurements were made for five minutes in the supine position and continued while the tilt table was raised to 80^{o} upright. The subject was kept in the upright position for ten minutes, after which a final blood sample was drawn for plasma norepinephrine and epinephrine levels. Echocardiographic images were recorded on videotape and analog data were recorded on digital tape and paper recorders for later analyses.

The following variables were compared during the last minute supine and the last minute standing: plasma norepinephrine and epinephrine levels; heart rate; systolic and diastolic pressures; stroke volume; cardiac output (stroke volume x heart rate); and total peripheral resistance (mean arterial pressure/cardiac output). Analyses of all signals were made by using standard data acquisition and analysis packages. Plasma norepinephrine and epinephrine levels were determined using a radioenzymatic assay (10).

Statistics

No statistical analyses were performed on the data from the elderly subject. Since the subject did not become presyncopal during tilt testing on any of the test days, his data are presented in comparison to those of 20 younger male astronauts (41 $\pm$ 1 years of age) who had previously participated in the same study (2) and who also did not become presyncopal. Data from the younger astronauts are presented as mean $\pm$ SEM. Female astronauts who had previously participated in this study were excluded based on the known gender differences in responses to orthostatic stress as well as their greater susceptibility to orthostatic hypotension after spaceflight (2).

RESULTS:

Plasma Volume

Plasma volumes are presented in Figure 1. There were no noticeable differences in preflight to landing day plasma volume changes between the younger and older astronauts.

Hemodynamic responses to standing

Figures 2 through 8 depict responses to standing in the younger group of astronauts and the elderly astronaut. Supine and standing mean arterial pressures were similar between the younger and older astronauts on all occasions (Fig. 2), although the older individual had somewhat higher pressures on landing day. The elderly subject however, had a hemodynamic profile that was very different from the younger subjects. There were several notable differences in his responses to standing. First, the elderly subject demonstrated larger increases in norepinephrine levels upon standing than the younger counterparts, most particularly on landing day (Fig. 3). Second, the elderly subject had markedly lower epinephrine levels on all occasions than the younger astronauts (Fig. 4). Third and fourth, in spite of his seemingly high sympathetic activation, the elderly subject showed virtually no increase in total peripheral resistance (Fig. 5), and minimal increases in heart rate (Fig. 6), with standing during all test sessions. In contrast, the younger astronauts had significant increases in resistance and heart rate upon standing. Finally, during all test sessions the elderly astronaut maintained upright stroke volume (Fig. 7) and cardiac output (Fig. 8) close to his supine levels, while the younger astronauts always sustained significant drops in standing stroke volumes and cardiac outputs.

DISCUSSION

This study was undertaken to compare the cardiovascular responses to standing before and after spaceflight in an elderly astronaut and younger astronauts. The differences observed are similar to known differences between healthy elderly and younger men in the general population. While the elderly astronaut maintained arterial pressures that were similar to those of -the younger group, his hemodynamic profile was quite different, and typical of older individuals. These findings were consistent before and after flight, and suggest that the older astronaut was not differentially affected by spaceflight.

Previous studies have documented important individual differences in the effects of spaceflight on astronauts. Those who become presyncopal during upright posture after landing consistently have shown low standing total peripheral resistance (2,11), and plasma norepinephrine levels (2,12). In contrast, astronauts who do not become presyncopal on landing day mount hyperadrenergic responses (2,13,14) on landing day and increase standing peripheral resistance adequately. In the present study, the elderly male astronaut did not become presyncopal. Therefore, we chose to compare his data only to data from a group of younger male astronauts who also had not become presyncopal, thus eliminating gender as a factor. This comparison revealed important differences between the older and younger men.

A striking finding from this study was the dramatic increase in standing norepinephrine levels in the elderly subject on landing day, which was greater than that of any other subject. This seems to be consistent with his age. Aging is associated with

high plasma norepinephrine levels at rest (15-19) and in response to mental stress (20), hypoglycemia (21), exercise (22,23) and upright posture (24,25). In addition, directly recorded sympathetic nerve traffic is increased in the elderly (26-29). Some authors have suggested that increases in sympathetic drive with age may be the result of impairment of inhibitory baroreceptor input (26,30,31). Supporting this idea is a study which showed that aging leads to decreased tonic vagal restraint on sympathetic nerve activity (32). Epinephrine levels have not been shown to increase with aging (19), also consistent with the present findings.

The high standing plasma norepinephrine levels in the elderly subject in the present study did not translate into substantial increases in either heart rate or total peripheral resistance. This pattern persisted during every test session. This cardiac finding also is consistent with findings from studies on the elderly, which report reductions in both inotropic and chronotropic responses. For example, increases in heart rate during exercise (18,33,34) or as a baroreflex mediated response to the α-1 antagonist, prazosin (35) both are decreased in the elderly. Increases in left ventricular contractility during exercise (36) also are reduced. One factor which may contribute to this incongruence between norepinephrine release and cardiac responses is that aging is associated with β-adrenergic receptor dysfunction. Cardiac responses to β-adrenergic agonists such as isoproterenol are reduced in the elderly (18,37-41). In addition, the affinity for isoproterenol of β-receptors on lymphocytes is reduced in elderly humans (42), and in senescent rats the density of myocardial β-receptors is decreased (43). Reductions in responsiveness of β-receptors actually may be a primary change associated

with aging that is not caused by disease or inactivity (44,45). Therefore, we suggest that the lack of heart rate response in the presence of high plasma norepinephrine levels in this healthy subject is due to age-related reductions in receptor responsiveness. This response was not affected by spaceflight and we suggest it is not abnormal for an elderly subject.

High norepinephrine levels in this elderly astronaut also did not translate into large increases in total peripheral resistance with standing. This also may be explained by age associated changes in adrenergic receptors. Although there have been fewer studies on aging and α-adrenergic receptors, it is known that pressor responses to phenylephrine, an α-1 specific agonist, are reduced in elderly humans (35) and platelet α_2 receptor numbers are lower (16). Thus arteriolar vasoconstriction is likely to be compromised, limiting the ability to increase resistance with increases in norepinephrine. As mentioned above, the ability to maintain standing pressure on landing day seems to be dependent on a hyperadrenergic response. The elderly subject in this study displayed the ability to release very large amounts of norepinephrine on landing day.

As mentioned earlier, standing stroke volume was maintained in the older astronaut during all test sessions. This finding also is consistent with the aging literature. It has been shown that stroke volume is maintained better in elderly men than in young men during stand tests (46). Furthermore, during exercise, cardiac output is maintained with a lower heart rate, higher end diastolic volume and higher stroke volume in elderly

versus younger subjects (47). In that study the older subjects maintained higher venous return and relied more heavily on the Frank-Starling mechanism to maintain cardiac output. Other mechanisms also may help to explain why venous return is so well maintained in the aged. Elderly subjects have decreased venous capacitance secondary to vessel stiffening (48) and reduced venous distensibility at rest and in response to nitroglycerin (49) and lower body negative pressure (50). It has been suggested that this decrease may occur secondarily to an increase in the collagen/elastin ratio and/or venous wall thickening. These changes would be expected to discourage venous pooling during upright posture and may help explain the current findings.

In summary, a 77 year old male astronaut underwent tilt tests before and after spaceflight and did not become presyncopal during any test session. He experienced arterial pressures which were very similar to those of younger astronauts. However, the hemodynamic strategies he employed were very different from the younger astronauts, but typical of those in the geriatric population. His responses did not seem to be deleteriously affected by spaceflight. This subject's excellent physical condition as a geriatric athlete allowed him to endure the rigors of spaceflight, but did not allow him to escape all the physiological effects of aging. These data suggest that elderly individuals who maintain their health and fitness are able to withstand the stresses of extreme environments and do not necessarily need to limit their activities simply due to their chronological age.

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FIGURE LEGENDS

Figure 1. Supine plasma volumes before and after spaceflight in 20 younger astronauts and one elderly astronaut.

Figure 2. Supine and standing mean arterial pressures before flight, on landing day and three days after landing in 20 younger astronauts and one elderly astronaut. The elderly astronaut showed no evidence of an inability to maintain standing arterial pressure.

Figure 3. Supine and standing plasma norepinephrine levels before flight, on landing day and three days after landing in 20 younger astronauts and one elderly astronaut. The elderly astronaut had extraordinarily high levels of norepinephrine on landing day. ** = $P< 0.001$

Figure 4. Supine and standing plasma epinephrine levels before flight, on landing day and three days after flight in 20 younger astronauts and one elderly astronaut. Low epinephrine levels were noted in the elderly astronaut on all occasions. * = $P<0.05$, **=$P<0.01$

Figure 5. Supine and standing total peripheral resistance before flight, on landing day and three days after landing in 20 younger astronauts and one elderly astronaut. While the younger astronauts had significant increases in resistance with standing on all occasions, the elderly astronaut had very small changes in resistance. ** = $P < 0.001$

Figure 6. Supine and standing heart rates before flight, on landing day and three days after landing in 20 younger astronauts and one elderly astronaut. While the younger astronauts showed significant increases in heart rate with standing on all occasions, the elderly astronaut had only small increases in heart rate. ** = $P < 0.001$

Figure 7. Supine and standing stroke volumes before flight on landing day and three days after landing in 20 younger astronauts and one elderly astronaut. The younger astronauts had significantly smaller stroke volumes standing than supine on all occasions. In contrast, the elderly astronaut had very little loss of stroke volume with standing. ** = $P < 0.001$

Figure 8. Supine and standing cardiac outputs before flight, on landing day and three days after landing in 20 younger astronauts and one elderly astronaut. During all test sessions the elderly astronaut maintained standing cardiac output well, while the younger astronauts had significant falls in cardiac output. ** = $P < 0.001$

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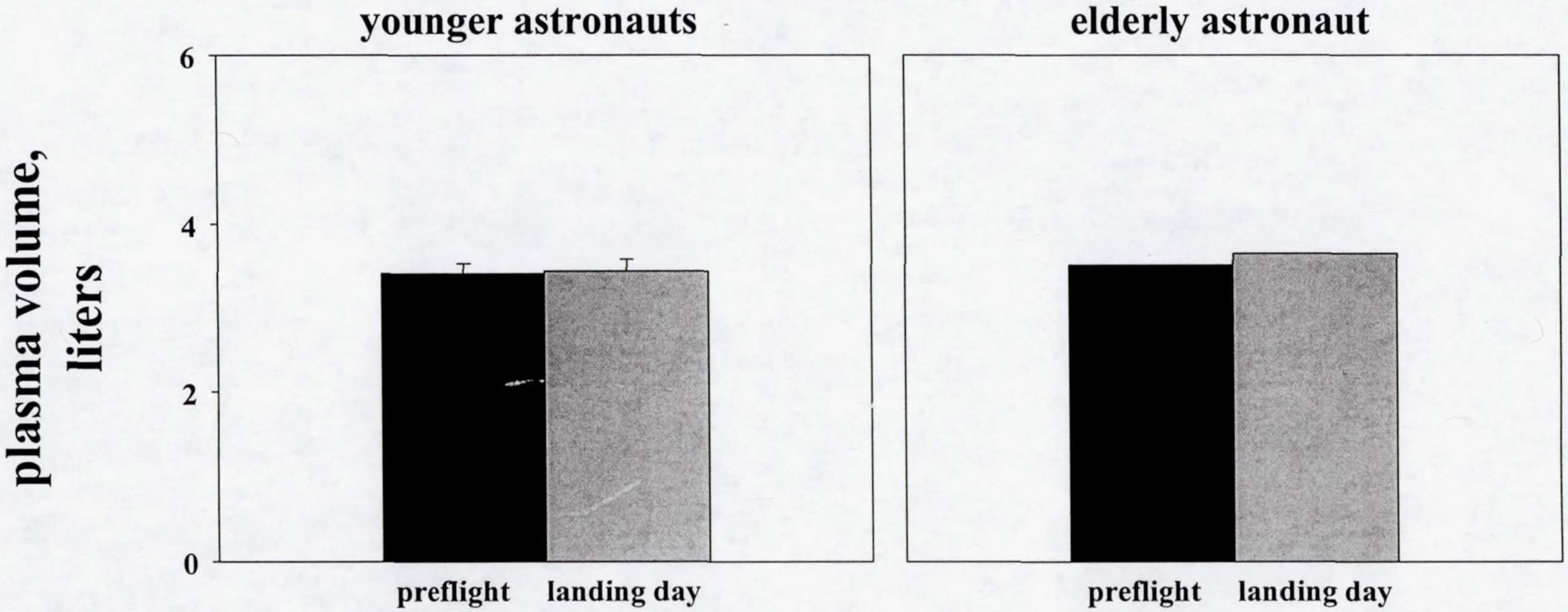
Miniabstract

We studied neuroendocrine and hemodynamic responses to standing before and after spaceflight in a 77 year old male astronaut and compared them to those of 20 younger astronauts. With standing, the older astronaut had greater maintenance of stroke volume and cardiac output, larger increases in plasma norepinephrine levels, but smaller increases in heart rate and peripheral resistance than the younger astronauts a pattern typical of the geriatric population.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elderly astronaut
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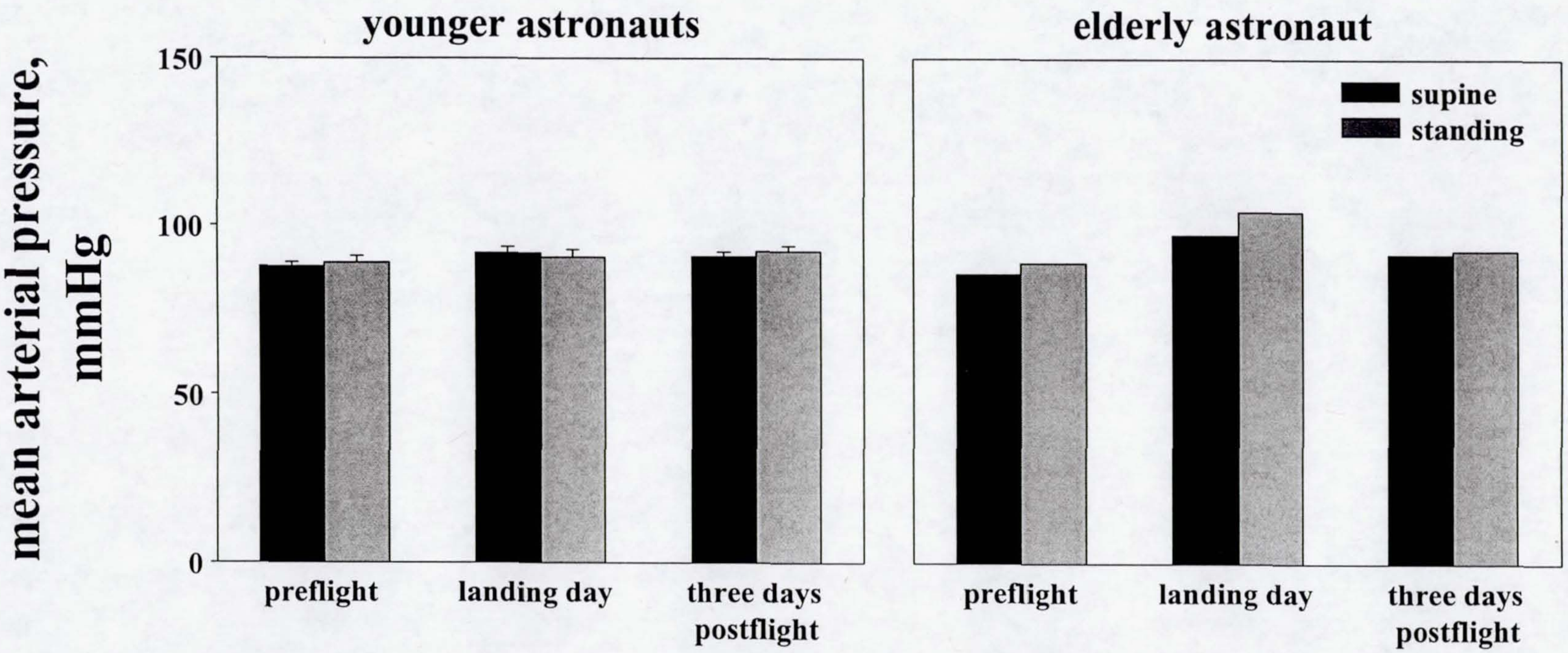
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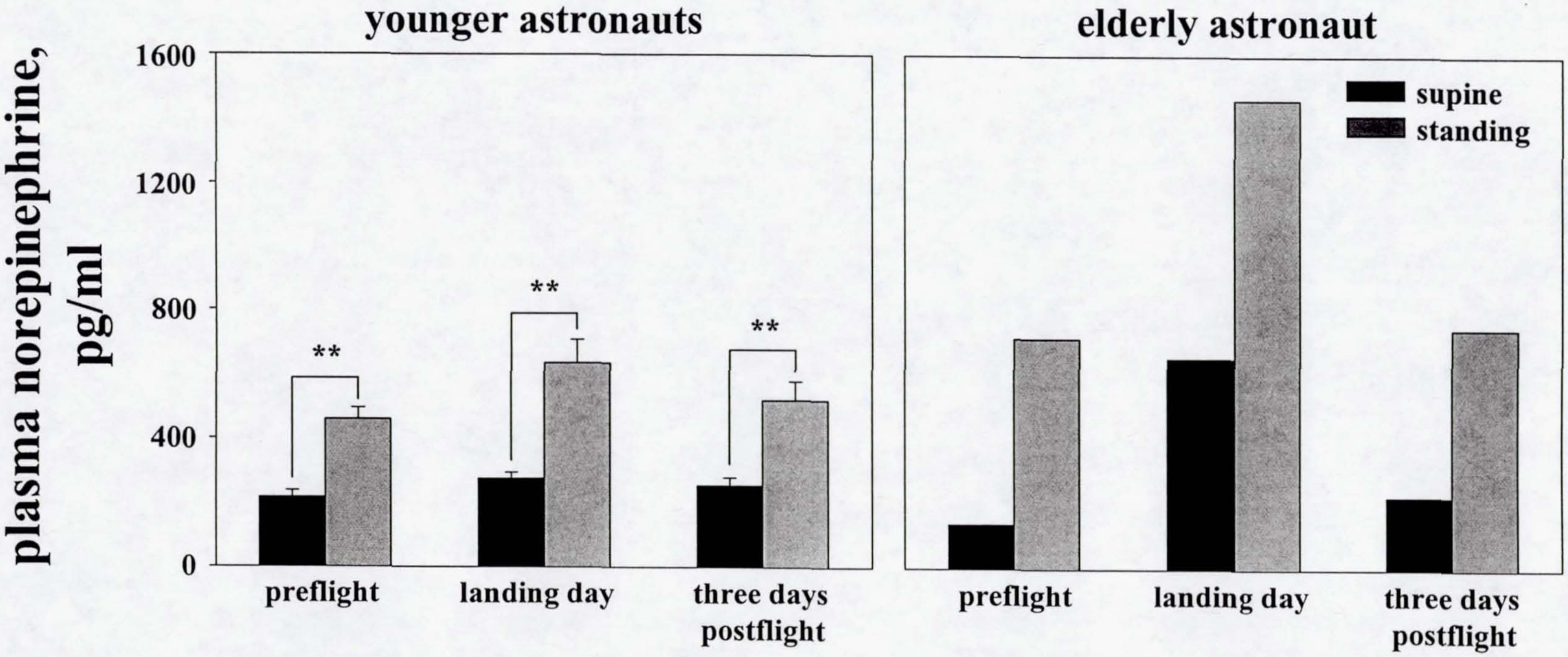
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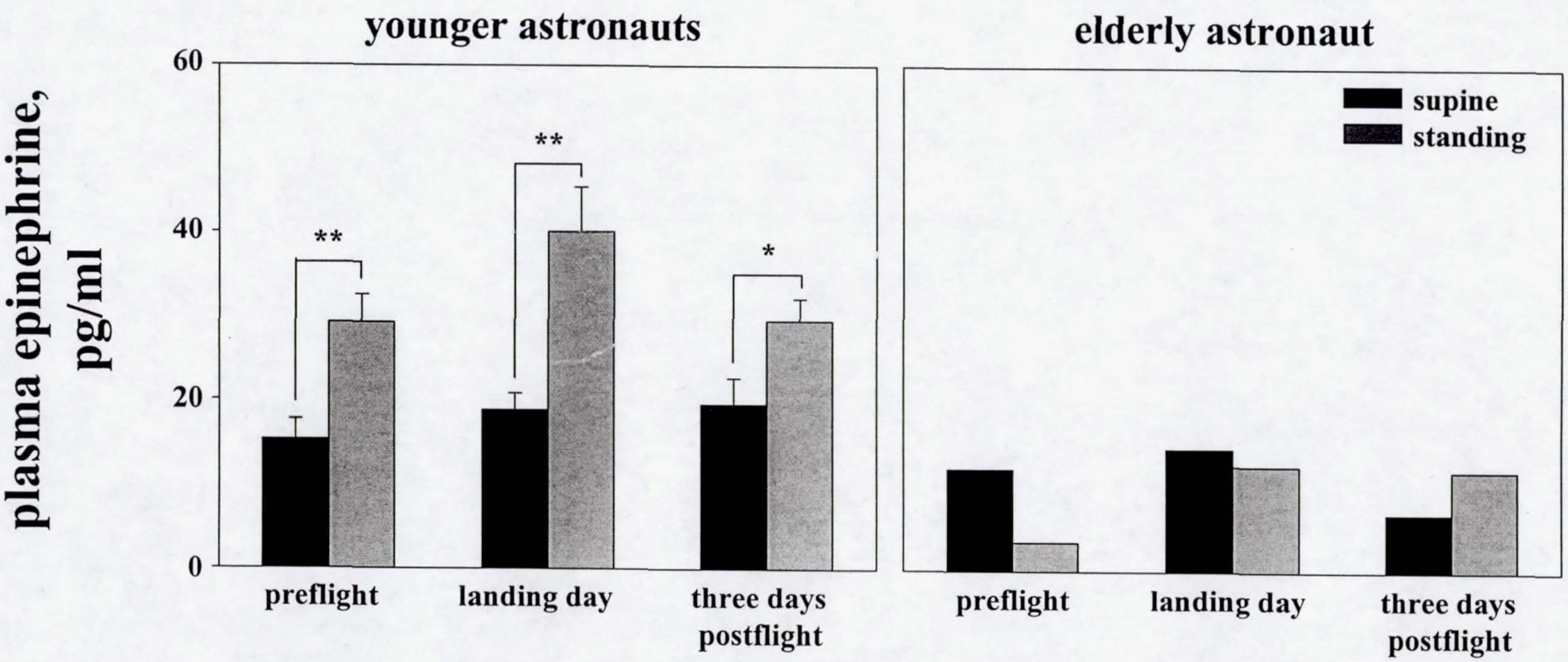
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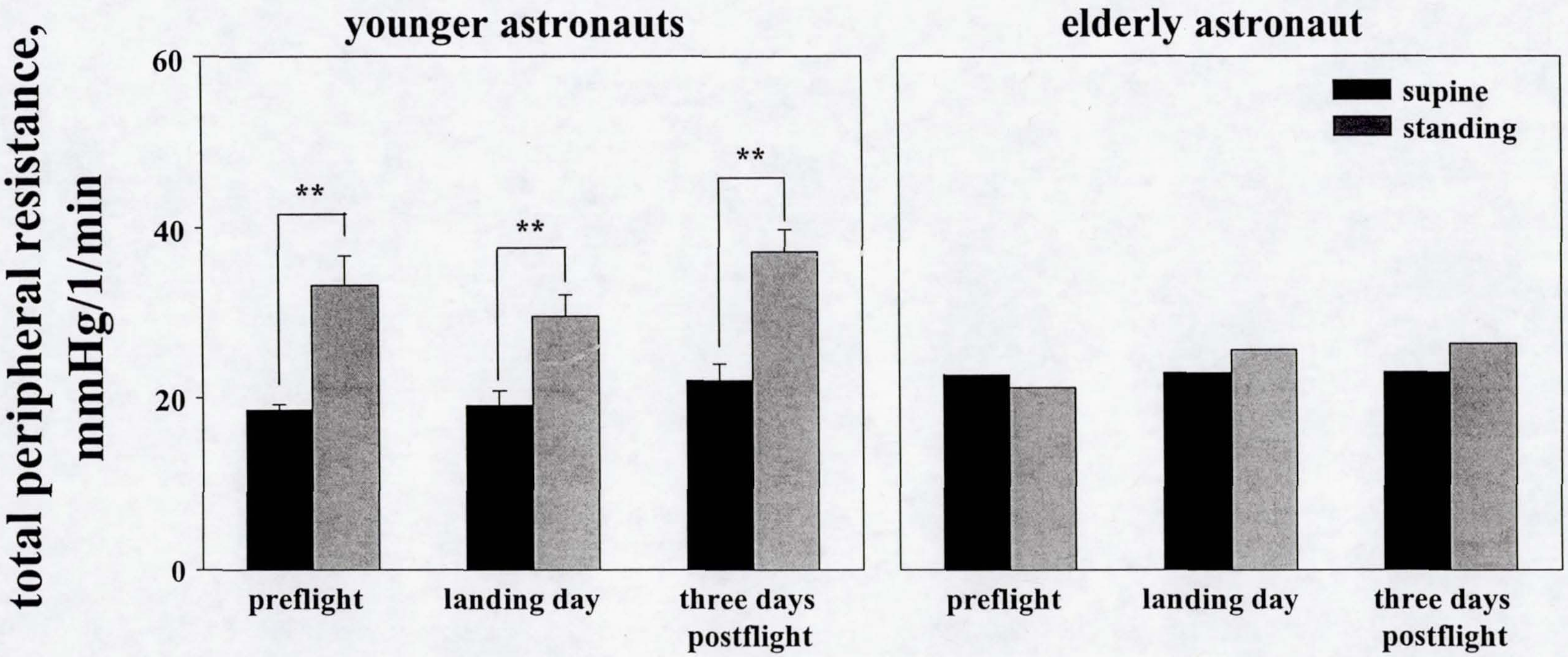
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elderly astronaut
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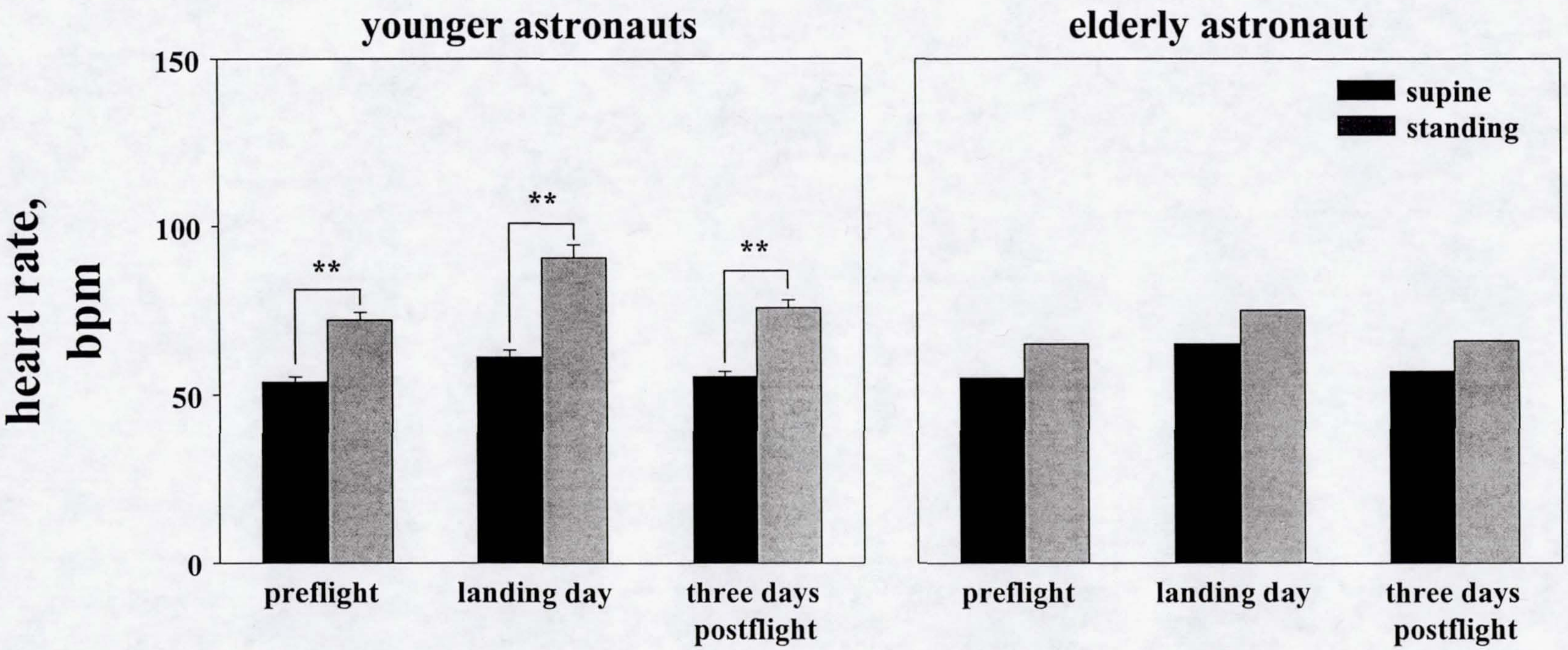

younger astronauts
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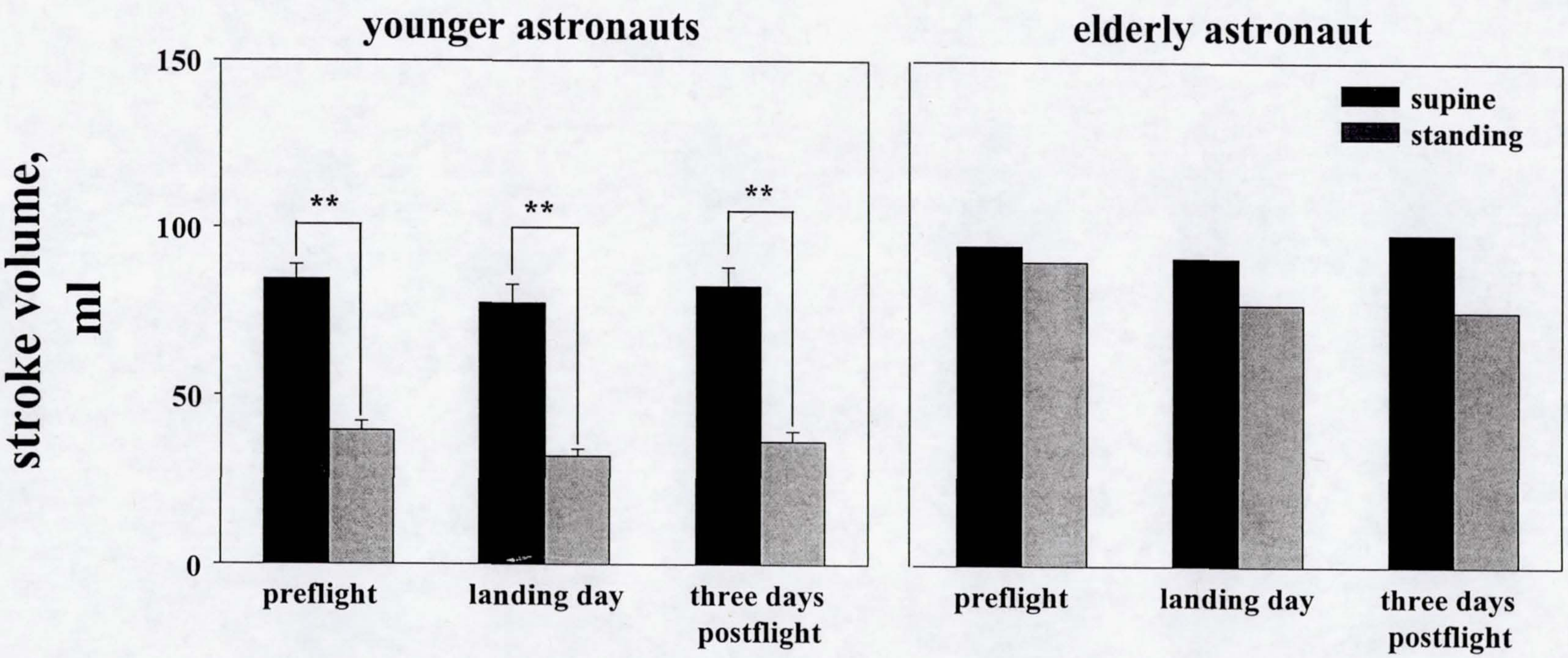

younger astronauts
elderly astronaut
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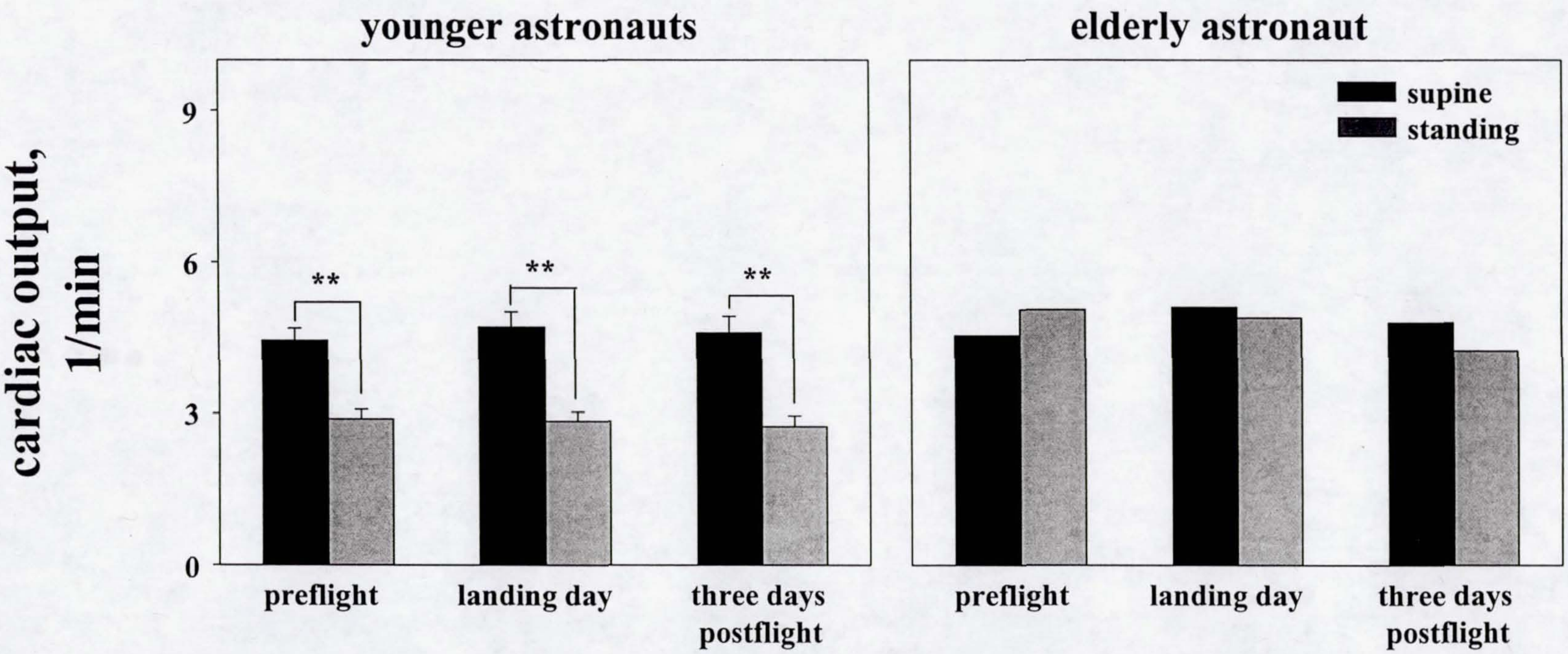

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